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Ayesha C. Sujan, M.A.,[a] Martin E. Rickert, Ph.D.,[a] A. Sara Öberg, M.D., Ph.D.,[b,c] Patrick D. Quinn, Ph.D.,[a] Sonia Hernández-Díaz, M.D., Ph.D.,[c] Catarina Almqvist, M.D., Ph.D.,[b] Paul Lichtenstein, Ph.D.,[b] Henrik Larsson, Ph.D.,[b,d] and Brian M. D'Onofrio, Ph.D.[a, b, e]

[a]Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, USA

[b]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

[c]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, USA

[d] School of Medical Sciences, Örebro University, Örebro, Sweden

[e]All correspondence should be sent to:

Brian M. D'Onofrio

Department of Psychological and Brain Sciences

Indiana University

1101 E. 10th St.

Bloomington, IN 47405

Phone: 812-856-0843

Fax: 812-856-4544

bmdonofr@indiana.edu

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Key Points

Question: Is first-trimester maternal antidepressant use related to offspring birth and/or neurodevelopmental problems? **Findings:** In this retrospect cohort study of 1,580,629 Swedish offspring using multiple statistical and methodical approaches to adjust for confounding, first-trimester antidepressant exposure was significantly associated with preterm birth (OR = 1.3 in a sibling comparison analysis) but not with risk of being born small for gestational age or later autism spectrum disorder or attention-deficit/hyperactivity disorder. **Meaning:** After accounting for confounding factors, first-trimester antidepressant exposure, compared with no exposure, was associated with a small increased risk of preterm birth but no increased risk of small for gestational age, autism spectrum disorder, or attention-deficit/hyperactivity disorder.

Abstract

Importance: Prenatal antidepressant exposure has been associated with adverse outcomes. Previous studies, however, may not have adequately accounted for confounding.

Objective: To evaluate alternative hypotheses for associations between first-trimester antidepressant exposure and birth and neurodevelopmental problems.

Design, Setting, and Participants: This retrospective cohort study included Swedish offspring born between 1996 and 2012 and followed through 2013 or censored by death or emigration. Analyses controlling for pregnancy, maternal, and paternal covariates, as well as sibling comparisons, timing of exposure comparisons, and paternal comparisons, were used to examine the associations.

Exposures: Maternal self-reported first-trimester antidepressant use and first-trimester antidepressant dispensations.

Main Outcomes and Measures: Preterm birth (< 37 gestational weeks), small for gestation age (birth weight < 2 SDs below the mean for gestational age), and first inpatient or outpatient clinical diagnosis of autism spectrum disorder and attention-deficit/hyperactivity disorder in offspring.

Results: Among 1,580,629 offspring (mean gestational age 279 days; 48.6% female; 1.4% [n = 22,544] with maternal first-trimester self-reported antidepressant use) born to 943,776 mothers (mean age at childbirth 30 years), 7.0% of exposed vs. 4.8% of unexposed offspring were preterm, 2.5% of exposed vs. 2.2% of unexposed were small for gestational age, 5.3% of exposed vs. 2.1% of unexposed were diagnosed with autism spectrum disorder by age 15, and 12.6% of exposed vs. 5.5% of unexposed were diagnosed by attention-deficit/hyperactivity disorder by age 15. At the population level, first-trimester exposure was associated with all

outcomes, compared with unexposed offspring (preterm birth: OR = 1.5, 95% CI, [1.4, 1.6]; small for gestational age: OR = 1.2, 95% CI, [1.1, 1.3]; autism spectrum disorder: HR = 2.0, 95% CI, [1.8, 2.3]; attention-deficit/hyperactivity disorder: HR = 2.2, 95% CI, [2.0, 2.4]). However, in models that compared siblings while adjusting for pregnancy, maternal, and paternal traits, first-trimester antidepressant exposure was associated with preterm birth (OR = 1.3, 95% CI [1.2, 1.5]) but not with small for gestational age (OR = 1.0, 95% CI [0.8, 1.3]), autism spectrum disorder (HR = 0.8, 95% CI [0.6, 1.1]), or attention-deficit/hyperactivity disorder (HR = 1.0, 95% CI [0.8, 1.3]). Results from analyses assessing associations with maternal dispensations before pregnancy and paternal first-trimester dispensations were consistent with findings from the sibling comparisons.

Conclusion and Relevance: Among offspring born in Sweden, after accounting for confounding factors, first-trimester antidepressant exposure, compared to no exposure, was associated with a small increased risk of preterm birth but no increased risk of small for gestational age, autism spectrum disorder, or attention-deficit/hyperactivity disorder.

Given the increasing prevalence of antidepressant use among pregnant women,[1] gaining knowledge on the safety of their use during pregnancy is a public health priority. Prenatal antidepressant exposure is associated with birth and neurodevelopmental problems, including shorter gestation,[2] reduced fetal growth,[2] autism spectrum disorder,[3-6] and attention-deficit/hyperactivity disorder.[7] These associations may be due to causal mechanisms (e.g., dysfunctional serotonin signaling[8]). However, there are alternative explanations for the associations. Maternal depression and stress are associated with birth[9] and neurodevelopmental[10] problems, suggesting that antidepressant associations could be attributable to confounding by indication for such treatment. Furthermore, autism spectrum disorder and attention-deficit/hyperactivity disorder have strong genetic influences,[11] and these influences partially overlap with genetic contributions to depression.[12,13] Thus, genetic transmission of shared risk for neurodevelopmental problems and depression could explain the associations (i.e., passive gene-environmental correlation). Other factors, such as poor health practices during pregnancy, could also account for the associations.[14]

Randomized clinical trials have not been able to test the safety of antidepressant use during pregnancy because pregnant women are typically excluded from these studies. Thus, researchers must use observational designs to rule out alternative explanations for the associations.[15] The present study used four such designs to explore associations between first-trimester antidepressant exposure (assessed via both maternal self-report and registered medication dispensations) and offspring birth and neurodevelopmental problem (i.e., preterm birth, small for gestational age, autism spectrum disorder, and attention-deficit/hyperactivity disorder. In addition to (1) statistical controls to adjust for measured pregnancy, maternal, and paternal characteristics, this study used (2) sibling comparisons to account for unmeasured

genetic and environmental factors that make siblings similar, (3) timing-of-exposure comparisons to account for selection factors related to maternal antidepressant treatment around the time of pregnancy, and (4) paternal comparisons to further account for familial confounding.

Methods

The institutional review board at Indiana University and the Regional Ethical Review Board in Stockholm approved this study. By Swedish law informed consent was not necessary because the study used data available from national registers.

Sample

We obtained a population-based dataset by linking information from the following Swedish registers: (1) the Multi-Generation Register, which included biological relationships for all individuals residing in Sweden since 1961, (2) the Prescribed Drug Register, which included prescription medication dispensation records since 2006, (3) the Medical Birth Register, which included information on 96-99% of births since 1973, (4) the National Patient Register, which included diagnoses from all hospital admissions since 1987 and specialist outpatient care since 2001, (5) the National Crime Register, which included criminal convictions since 1973, and (6) the Education Register, which included highest level of completed formal education through 2013.

Measures

Antidepressant exposure. The main exposures evaluated were first-trimester exposure to (1) any antidepressants (medications with Anatomical Therapeutic Chemical Classification [ATC] codes beginning with N06A) and (2) Selective Serotonin Reuptake Inhibitors (SSRIs; medications with ATC codes beginning with N06AB). Exposure was defined according to two sources of information: (1) maternal self-reports (available for offspring born between 1996 and

2012) and (2) dispensation records (available for both parents of offspring born between 2006 and 2012).

Information on maternal *self-reported* medication use during the first trimester of pregnancy came from the Medical Birth Register, which contains information obtained from standardized interviews conducted by midwives at the first antenatal visit. Medication reported in these interviewers is presumed to represent first-trimester use because interviews typically occur between week 10 and 12 of pregnancy.

Information on medication use based on *dispensation* records came from the Prescribed Drug Register, which covers all medication dispensations and accompanying prescriptions made in Sweden since July 2005. The only medication use not covered by the register is medication administered while in hospital, purchased over the counter, or obtained on the black market. The Prescribed Drug Register was used to obtain information on *maternal* antidepressant dispensations that covered the periods before pregnancy and during the first trimester of pregnancy and *paternal* antidepressants that covered the period during the first trimester of pregnancy. First-trimester exposure was defined as having at least one dispensation between 90 days before estimated conception and 90 days after estimated conception (see eFigure 1). The window included 90 days before conception because chronic disease medication is typically prescribed for at least 3-month periods in Sweden. Use before pregnancy only was defined as having at least one dispensation between 270 and 90 days before estimated conception and no dispensations during pregnancy or during the 180 days after delivery.

Main Outcomes. The birth outcomes were preterm birth (< 37 gestational weeks) and small for gestational age (birth weight < 2 SDs below the mean for gestational age). The neurodevelopmental outcomes were first diagnosis of autism spectrum disorder and attention-

deficit/hyperactivity disorder, which were identified using inpatient and outpatient diagnoses made by specialists according to *International Classification of Diseases, Ninth Revision* (ICD-9) and ICD-10 criteria. Previous research has validated these diagnoses in the Swedish registers.[16,17] Participants were followed through 2013 or were censored because of death or emigration. More details about the registers and variables are available in previous publications.[e.g.,18,19]

Covariates. Pregnancy covariates included parity (categorized as first, second, third, or fourth or higher) and year of birth. Maternal and paternal covariates included country of birth (Sweden or outside Sweden), age at childbearing (categorized into six levels), highest level of completed education (categorized into seven levels), history of any criminal conviction, history of severe psychiatric problems (inpatient diagnosis of ICD-8, ICD-9, or ICD-10 schizophrenia, bipolar disorder, or other non-drug-induced psychoses), and history of any suicide attempts (definite or uncertain). History of criminal convictions is commonly used in Swedish register studies to index problems with behavior regulation.[e.g.,20,21]

Analyses

We performed a complete-case analysis. We managed and analyzed data in SAS 9.4 and STATA 13.1 and calculated 95% confidence intervals based on two-sided hypothesis testing.

Descriptive statistics. We provided the distribution of covariates and outcomes in the whole sample and in the subsamples of exposed an unexposed offspring. In addition, we provided the occurrence of the outcomes and covariates in differentially exposed and unexposed siblings. For the birth outcomes, we presented proportions and unadjusted risk differences. We presented Kaplan Meier estimates of the probability of the neurodevelopmental diagnoses because follow-up time was censored.

Population-wide associations and within-family comparisons. Logistic regression was used to estimate the model-based associations for the two birth (i.e., binary response) outcomes. Cox proportional hazards regression (using calendar age in years as the timescale) was used to estimate the associations for the two neurodevelopmental outcomes to account for censored observations in the data. We examined the associations between antidepressant exposure and outcomes by estimating a sequence of three models with increasing degree of control for potential confounding factors. First, the baseline models assessed population-wide associations while only adjusting for pregnancy covariates (parity and year of birth). Second, the population-wide associations were further adjusted for all maternal and paternal covariates. These population models used robust standard errors to account for clustering of individuals (i.e., siblings) within nuclear families bound by the same biological mother. Third, sibling comparison models compared exposure and outcome discordant offspring within families and included covariates that could vary among siblings born to the same mother. By design, these models accounted for all factors that made siblings similar (e.g., shared genetic and early environmental influences), as well as measured covariates that vary within families, thereby producing a stronger test of the associations than the adjusted population models.[22] As recommended,[23] we fit fixed-effects models using conditional logistic and stratified Cox regression to make purely within-family comparisons.

Comparisons of timing of maternal use and paternal use. To explore whether intrauterine exposure was specifically associated with outcomes over and above maternal depression treatment around the time of pregnancy, we compared associations for maternal first-trimester antidepressant dispensations with associations for dispensations before pregnancy, while adjusting for measured pregnancy, maternal, and paternal covariates. We evaluated

whether these associations differed statistically using Wald χ^2 tests. We also compared the fit of models that included separate parameters for before pregnancy dispensations and first-trimester dispensations to models that included one parameter for both dispensation windows. In addition, paternal first-trimester antidepressant dispensations were used as a negative control to further explore the role of familial confounding. We first assessed the association between maternal and paternal first-trimester dispensations. We then estimated associations between paternal first-trimester antidepressant dispensations and the four outcomes while adjusting for the pregnancy covariates.

Sensitivity analyses. First, to evaluate the influence of exposure misclassification, we examined adjusted associations with five additional exposure definitions in the cohort with exposure information from both maternal self-reports and dispensations (i.e., the cohort born 2006 to 2012). The four additional definitions included: (a) first-trimester exposure defined as use according to *either* self-reports or dispensation records, (b) first-trimester exposure defined as use according to *both* self-reports and dispensation records, (c) a narrower first-trimester dispensation window of 30 days before conception to 90 days after conception, and (d) at least two dispensations during the original first-trimester exposure window. Second, given that single-offspring families cannot contribute to sibling-comparison analyses, we reassessed the population models in the subsample of offspring with siblings to evaluate the generalizability of sibling-comparison results. Third, to assess if exposure to other psychotropic medications confounded the associations, we restricted the analyses to offspring not exposed to other psychotropic medications. Fourth, given that prior to 2001 outpatient psychiatric diagnoses were not included in the National Patient Register, we conducted analyses on a subsample of offspring born after 2000 to assess whether left censoring of the neurodevelopmental outcomes biased the

findings. These analyses also enabled us to explore whether cohort effects influenced the results. Fifth, we estimated the associations with the neurodevelopmental outcomes in subsamples excluding offspring with diagnoses before age 2 to address concerns about the validity of early neurodevelopmental diagnoses. Sixth, because the main analyses focused on first-trimester exposure, we examined the association between dispensations during the second and/or third trimester and each outcome in the subsample of offspring whose mothers had a dispensation during the first trimester.

Results

The target sample included 1,670,237 offspring born 1996-2012. Multiple births (48,979 offspring), cases with missing father identifier (16,295), missing or invalid responses on covariates (20,118), and missing on the small for gestational age variable (4,216) were sequentially dropped. The final analytic cohort of 1,580,629 offspring (48.6% female) represented 95% of target singleton births and included 943,776 distinct mothers and 946,579 distinct fathers. According to maternal self-reports, 22,544 (1.4%) of the offspring in the final cohort were exposed to any antidepressant during the first trimester, and of these, 82% (18,470) were exposed to SSRIs.

The timing of exposure and paternal comparisons were conducted on the subsample of 708,450 offspring (born between 2006 and 2012) with dispensation-based exposure data. There were 26,477 (3.7%) offspring with first-trimester maternal antidepressant dispensations. Of these, 84% (22,125) had first-trimester maternal SSRI dispensations specifically. There were 8,203 (1.2%) offspring who had mothers with antidepressant dispensations before pregnancy only. Of these, 81% (6,674) had mothers who were specifically dispensed SSRIs before pregnancy. There were 18,727 (2.6%) offspring who had fathers with first-trimester

antidepressant dispensations. Of these, 72% (13,521) had fathers with first-trimester SSRI dispensations specifically.

The same pattern of results was observed for associations with first-trimester exposure to any antidepressant as first-trimester exposure to SSRIs specifically. Therefore, results for exposure to any antidepressant are presented in the text and tables. The results for SSRIs can be found in the tables and online supplement.

Descriptive Statistics Stratified By Maternal Self-reported Antidepressant Use

In the whole sample, 7.0% of exposed and 4.8% of unexposed offspring were preterm (Table 1), which equates to 220 (95% CI [187, 254]) additional preterm birth cases per 10,000 offspring. Approximately 2.5% of exposed and 2.2% of unexposed offspring were born small for gestational age, (risk difference = 35 additional cases per 10,000 offspring; 95% CI [14, 56]). Compared to unexposed offspring, exposed offspring also had a higher probability of the neurodevelopmental diagnoses (see Figure 1a and 1c for the Kaplan Meier estimates and confidence intervals). For example, by age 15, Kaplan Meier estimates indicated a cumulative risk of autism spectrum disorder of 5.3% for exposed and 2.1% for unexposed offspring. By age 15, the cumulative risk of attention-deficit/hyperactivity disorder was 12.6% for exposed and 5.5% for unexposed offspring. See eSupplement A for more descriptive information.

Among differentially exposed siblings, 6.2% of exposed and 5.1% of unexposed siblings were born preterm. However, 1.9% of exposed and 2.0% of unexposed siblings were small for gestational age. See Figure 1b and 1d for the probabilities of the neurodevelopmental diagnoses among differentially exposed siblings through age 15. By age 15, the cumulative risk for autism spectrum disorder was 5.5% for exposed and 4.6% for unexposed siblings; the cumulative risk

for attention-deficit/hyperactivity disorder was 12.4% for exposed and 12.7% for unexposed siblings.

Population-wide Associations and Sibling Comparisons

In the baseline models (Table 2), maternal self-reported first-trimester antidepressant use was associated with preterm birth (OR = 1.5, 95% CI [1.4, 1.6]), small for gestational age (OR = 1.2, 95% CI [1.1, 1.3]), autism spectrum disorder (HR = 2.0, 95% CI [1.8, 2.3]), and attention-deficit/hyperactivity disorder (HR = 2.2, 95% CI [2.0, 2.4]). In the adjusted models, first-trimester exposure to antidepressants was also statistically significantly associated with all outcomes (preterm birth OR = 1.4, 95% CI [1.3, 1.4]; small for gestational age OR = 1.1, 95% CI [1.0, 1.2]; autism spectrum disorder HR = 1.6, 95% CI [1.5, 1.8]; attention-deficit/hyperactivity disorder HR = 1.6, 95% CI [1.5, 1.7]).

In the sibling comparison models, first-trimester exposure was associated with preterm birth (OR = 1.3, 95% CI [1.2, 1.5], $p < 0.0001$). However, it was not associated with small for gestational age (OR = 1.0, 95% CI [0.8, 1.3]), autism spectrum disorder (HR = 0.8, 95% CI [0.6, 1.1]), or attention-deficit/hyperactivity disorder (HR = 1.0, 95% CI [0.8, 1.3]). See eSupplement A for information on offspring who could contribute to sibling comparison analyses.

Comparisons of Timing of Maternal Use and Paternal Use

Dispensation data was used in timing of exposure and paternal comparisons (see eSupplement B for more information). For preterm birth, the association with maternal dispensations before pregnancy but not during or after pregnancy (OR = 1.2, 95% CI [1.1, 1.3]; Table 3) was statistically significantly weaker than the association with first-trimester maternal dispensations (OR = 1.4, 95% CI [1.3, 1.5]). For all other outcomes, the associations with

maternal dispensations before but not during or after pregnancy did not statistically significantly differ from the associations with first-trimester maternal dispensations.

Paternal first-trimester antidepressant dispensations were associated with maternal first-trimester antidepressant dispensations (OR = 3.4, 95% CI [3.3, 3.6]). Paternal first-trimester antidepressant dispensations (Table 4) had very modest associations with preterm birth (OR = 1.1, 95% CI [1.1, 1.2]) and small for gestational age (OR = 1.1, 95% CI [1.0, 1.2]), with the latter not being statistically significant. Paternal dispensations during pregnancy were associated with autism spectrum disorder (HR = 1.3, 95% CI [1.1, 1.6]), and attention-deficit/hyperactivity disorder (HR = 1.7, 95% CI [1.4, 2.2]).

Sensitivity Analyses

Sensitivity analyses showed a consistent pattern of results across analyses using stricter criteria for exposure and narrower exposure windows, suggesting that exposure misclassification was not responsible for the pattern of findings (eSupplement C). Results from population models conducted on a subsample that excluded offspring who did not have siblings also were essentially identical to the main results (eSupplement D). These results provide support for the generalizability of sibling comparison results. Sensitivity analyses also suggested that confounding by exposure to other psychotropic medications (eSupplement E); left censoring of the neurodevelopmental outcomes and cohort effects (eSupplement F); and measurement error of the neurodevelopmental outcomes (eSupplement G) had very little influence on the results. In addition, among offspring whose mothers had a dispensation during the first trimester, a dispensation during the second or third trimester was associated with increased risk of the pregnancy outcomes, though the associations with the neurodevelopmental diagnoses were not statistically significant (eSupplement H).

Discussion

The present study found that, after accounting for measured pregnancy, maternal, and paternal traits, as well as all (unmeasured) stable familial characteristics shared by siblings, maternal antidepressant use during the first trimester of pregnancy, compared to no exposure, was associated with a small increased risk of preterm birth but no increased risk of small for gestational age, autism spectrum disorder, or attention-deficit/hyperactivity disorder. That is, unexposed siblings were at equal risk for small for gestational age, autism spectrum disorder, and attention-deficit/hyperactivity disorder as their exposed siblings. These results are consistent with the hypothesis that genetic and/or familial environmental factors account for the population-wide associations between first-trimester antidepressant exposure and these outcomes. Moreover, results from analyses examining timing of exposure were consistent with the interpretation of the sibling-comparison findings. Specifically, the strength of the associations between antidepressant dispensations before pregnancy and small for gestational age, autism spectrum disorder, and attention-deficit/hyperactivity disorder did not statistically significantly differ from that of associations for first-trimester antidepressant dispensations, suggesting that the underlying condition, rather than exposure to antidepressants during the first trimester, explained the associations. Paternal first-trimester antidepressant dispensations were also associated with the neurodevelopmental disorders. Because paternal antidepressant use during the first trimester is unlikely to contribute to intrauterine exposure, these findings provide further support that associations between first-trimester antidepressant exposure and offspring neurodevelopmental problems may, at least partially, be explained by familial confounding.

The results also showed that, across multiple designs that account for familial confounding factors, first-trimester antidepressant exposure was associated with a slightly

elevated risk of preterm birth. Although these results may be consistent with the hypothesis that prenatal antidepressant exposure could lead to a small increased risk of preterm birth, other possible explanations for the findings need to be considered. Most important, the potential role of confounding by maternal depression should be noted because both the existence and severity of depression symptoms in the mother could potentially influence the risk of preterm birth.[24]

The results of the population-wide models were consistent with numerous observational studies that have demonstrated associations between prenatal antidepressant exposure and birth and neurodevelopmental problems.[2-7] The results of the sibling comparisons were also consistent with the limited previous sibling-comparisons studies that have examined associations between prenatal antidepressant exposure and birth and neurodevelopmental problems. A sibling comparison study using dispensation data from the Swedish registers found a statistically significant associations between prenatal antidepressant dispensations and shorter gestation.[25] Another sibling comparison reported that prenatal antidepressant exposure was not associated with autism spectrum disorder,[26] although confidence intervals were too wide to draw strong conclusions.

The current study had several strengths. First, the study analyzed a large, population-based sample, which provided statistical power to examine rare-yet-serious outcomes. Second, the conclusions were based on converging evidence from multiple research designs that accounted for both measured and unmeasured confounding factors. Third, first-trimester antidepressant use was indexed by both maternal self-report and dispensations. Fourth, the study included four outcomes, two pregnancy-related and two neurodevelopmental problems, all of which are associated with significant morbidity and mortality. Fifth, sensitivity analyses suggested that misclassification of antidepressant use, several assumptions of sibling-comparison

analyses, confounding by other psychotropic medications, and misclassification of the neurodevelopmental problems were unlikely to influence the overall conclusions.

The findings from the present study should be considered in light of several limitations. First, and most important, observational designs such as these cannot fully rule out all sources of confounding. In particular, like other register-based approaches,[26] this study could not comprehensively assess maternal depression or its severity,[27] nor could it compare different antidepressant treatment regimes. Thus, associations could have been influenced by confounding by antidepressant indication. In order to address this limitation, the study used multiple designs, each of which could help rule out some but not all sources of confounding, to provide complementary evidence. For example, sibling comparisons ruled out all stable confounders (e.g., chronic maternal depression), but that design may not have been able to account for confounding from maternal depression that varied across pregnancies.[28] Thus, the within-family associations with preterm birth may plausibly be driven by unmeasured time-varying maternal depression rather than by antidepressant use.[29]

Second, this study focused on first-trimester exposure. Whereas one recent study found an association between antidepressant dispensations late—but not early—in pregnancy and autism spectrum disorder,[3] there has been considerable debate regarding the role of timing.[30-32] In fact, several studies have found stronger associations with first-trimester antidepressant use than with use later in pregnancy.[4,6] Supplemental analyses indicated that among offspring whose mothers had a dispensation during the first trimester, a dispensation during the second or third trimester was associated with greater risk of offspring being born preterm and small for gestational age. These associations could be due to intrauterine exposure to antidepressants later in pregnancy, increased severity of depression (i.e., confounding by indication), or other

unmeasured confounding. Future studies are, therefore, needed to explicitly examine whether timing of exposure moderates the preterm birth association or whether exposure later in pregnancy is more strongly associated with other outcomes.

Third, the vast majority of antidepressant exposure (82% according to maternal reports) was to SSRIs. Future research should explore class- and drug-specific associations. Fourth, analyses were conducted on a Swedish sample, and it is not known if results would generalize to other countries. Although the population-wide associations in the present study were commensurate with those from other countries, future research should use designs that help account for unmeasured confounders to explore associations with prenatal antidepressant exposure in the United States and elsewhere. Fifth, sibling comparisons require large samples to have adequate statistical power.[33] Although the large Swedish sample ensured fairly precise parameter estimates in sibling comparisons, small effects of antidepressant exposure cannot be ruled out. However, their magnitudes, particularly for the neurodevelopmental outcomes, would be much smaller than those suggested by population-wide associations.

Conclusion

Among offspring born in Sweden, after accounting for confounding factors, first-trimester exposure to antidepressants, compared to no exposure, was associated with a small increased risk of preterm birth but no increased risk of small for gestational age, autism spectrum disorder, or attention-deficit/hyperactivity disorder.

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Figure 1. Risk of Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder by Maternal Self-reported First-trimester Exposure. The figure shows Kaplan-Meier estimates of cumulative risk (i.e., proportion diagnosed with) the neurodevelopmental outcomes (y-axis) by age (x-axis) among offspring with and without maternal self-reported first-trimester antidepressant exposure. The blue line shows exposed offspring. The black line shows unexposed offspring. Shaded areas around the blue and black lines are pointwise 95% confidence intervals. Top panels (A and B) show risk for autism spectrum disorder. Bottom panels (C and D) show risk for attention-deficit/hyperactivity disorder. Left panels (A and C) include the full cohort. Right panels (B and D) include siblings discordant for first-trimester antidepressant exposure. The median and interquartile range (IQR) follow-up time in the study (i.e., age since birth in years) were estimated separately for each exposure group. The median follow-up for autism spectrum disorder in the full cohort was 8.71 y [IQR: (4.69, 13.19)] for the unexposed group, and 5.82 y [IQR: (3.32, 9.08)] for the exposed group. The median follow-up for autism spectrum disorder in the sample of discordant siblings was 9.24 y [IQR: (5.54, 12.96)] for the unexposed group, and 6.27 y [IQR: (3.77, 9.02)] for the exposed group. The median follow-up for attention-deficit/hyperactivity disorder in the full cohort was 8.54 y [IQR: (4.54, 13.54)] for the unexposed group, and 5.54 y [IQR: (3.54, 9.54)] for the exposed group. The median follow-up for attention-deficit/hyperactivity disorder in the sample of discordant siblings was 9.54 y [IQR: (5.54, 13.54)] for the unexposed group, and 6.54 y [IQR: (3.54, 9.54)] for the exposed group.

Table 1. Descriptive statistics in the whole sample and stratified by maternal self-reported first-trimester use of any antidepressant

	Whole sample (n=1,580,629)	**Exposed offspring** (n=22,544)	**Unexposed offspring** (n=1,558,085)
	No. (%)	**No. (%)**	**No. (%)**
Offspring outcomes			
Preterm birth	76061 (4.81)	1574 (6.98)	74487 (4.78)
Small for gestational age	34728 (2.20)	573 (2.54)	34155 (2.19)
Autism spectrum disorder[a]	14617 (2.16)	299 (5.28)	14318(2.14)
Attention-deficit/hyperactivity disorder[a]	32924 (5.51)	613 (12.63)	32311(5.46)
Pregnancy covariates			
First born	693070 (43.85)	10467 (46.43)	682603 (43.81)
Second born	585619 (37.05)	6891 (30.57)	578728 (37.14)
Third born	213382 (13.50)	3463 (15.36)	209919 (13.47)
Fourth born or higher	88558 (5.60)	1723 (7.64)	86835 (5.57)
Born 1996 to 1999[b]	333791 (21.12)	1649 (7.31)	332142 (21.32)
Born 2000 to 2003[b]	349143 (22.09)	3004 (13.33)	346139 (22.22)
Born 2004 to 2007[b]	386511 (24.45)	6349 (28.16)	380162 (24.40)
Born 2008 to 2012[b]	511184 (32.34)	11542 (51.20)	499642 (32.07)
Maternal covariates			
Age at birth			
< 20 years	25637 (1.62)	327 (1.45)	25310 (1.62)
20 to 24 years	210552 (13.32)	2636 (11.69)	207916 (13.34)
25 to 29 years	495050 (31.32)	6124 (27.16)	488926 (31.38)
30 to 34 years	544746 (34.46)	7599 (33.71)	537147 (34.47)
35 to 39 years	254771 (16.12)	4730 (20.98)	250041 (16.05)
≥ 40 years	49873 (3.16)	1128 (5.00)	48745 (3.13)
Education			
Primary and lower secondary, < 9 years	33648 (2.13)	180 (0.80)	33468 (2.15)
Primary and lower secondary, 9 years	107953 (6.83)	2684 (11.91)	105269 (6.76)
Upper secondary, 1-2 years	246415 (15.59)	3852 (17.09)	242563 (15.57)
Upper secondary, 3 years	414949 (26.25)	6053 (26.85)	408896 (26.24)
Post-secondary, < 3 years	224706 (14.22)	3012 (13.36)	221694 (14.23)
Post-secondary, ≥ 3 years	533710 (33.77)	6585 (29.21)	527125 (33.83)
Postgraduate	19248 (1.22)	178 (0.79)	19070 (1.22)
Nationality (Swedish)	1281142 (81.05)	20361 (90.32)	1260781 (80.92)
Criminal convictions (any)	173631 (10.98)	3973 (17.62)	169658 (10.89)
Severe psychiatric problem[c]	16736 (1.06)	1734 (7.69)	15002 (0.96)
Suicide attempt (definite or uncertain)	66655 (4.22)	3251 (14.42)	63404 (4.07)
Paternal covariates			
Age at birth			
< 20 years	7789 (0.49)	134 (0.59)	7655 (0.49)
20 to 24 years	100339 (6.35)	1543 (6.84)	98796 (6.34)
25 to 29 years	364992 (23.09)	4815 (21.36)	360177 (23.12)
30 to 34 years	547663 (34.65)	7118 (31.57)	540545 (34.69)
35 to 39 years	355300 (22.48)	5380 (23.86)	349920 (22.46)
≥ 40 years	204546 (12.94)	3554 (15.76)	200992 (12.90)
Education			
Primary and lower secondary, < 9 years	29369 (1.86)	257 (1.14)	29112 (1.87)
Primary and lower secondary, 9 years	153577 (9.72)	2672 (11.85)	150905 (9.69)

Upper secondary, 1-2 years	403919 (25.55)	5647 (25.05)	398272 (25.56)
Upper secondary, 3 years	381746 (24.15)	6271 (27.82)	375475 (24.10)
Post-secondary, < 3 years	233560 (14.78)	2930 (13.00)	230630 (14.80)
Post-secondary, ≥ 3 years	348397 (22.04)	4404 (19.54)	343993 (22.08)
Postgraduate	30061 (1.90)	363 (1.61)	29698 (1.91)
Nationality (Swedish)	1273973 (80.60)	19699 (87.38)	1254274 (80.50)
Criminal convictions (any)	582002 (36.82)	9313 (41.31)	572689 (36.76)
Severe psychiatric problem[c]	10373 (0.66)	321 (1.42)	10052 (0.65)
Suicide attempt (definite or uncertain)	64879 (4.10)	1364 (6.05)	63515 (4.08)

All percentages are based on the number of offspring. [a]Age 15 Kaplan Meier estimates. [b]Year of birth is presented in bins in Table 1 but was not binned when used as a covariate in models. [c]Severe psychiatric problem was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

Table 2. Baseline, adjusted, and sibling comparison associations between maternal self-reported first-trimester use and birth and neurodevelopmental outcomes

	Baseline Model		Adjusted Model		Sibling Comparison	
Any antidepressant						
	OR	**95% CI**	**OR**	**95% CI**	**OR.**	**95% CI**
Preterm birth	1.47	1.40-1.55	1.35	1.28-1.42	1.34	1.18-1.52
Small for gestational age	1.15	1.06-1.25	1.12	1.03-1.22	1.01	0.81-1.25
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Autism spectrum disorder	2.02	1.80-2.26	1.64	1.46-1.83	0.83	0.62-1.13
Attention-deficit/hyperactivity disorder	2.21	2.04-2.39	1.58	1.46-1.71	0.99	0.79-1.25
SSRIs						
	OR	**95% CI**	**OR**	**95% CI**	**OR.**	**95% CI**
Preterm birth	1.38	1.30-1.46	1.27	1.20-1.35	1.33	1.16-1.53
Small for gestational age	1.11	1.01-1.21	1.09	0.99-1.20	0.88	0.70-1.12
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Autism spectrum disorder	2.04	1.80-2.32	1.66	1.46-1.89	0.81	0.58-1.14
Attention-deficit/hyperactivity disorder	2.25	2.06-2.46	1.60	1.47-1.75	0.94	0.73-1.22

OR = odds ratio. HR = hazard ratio. CI = confidence interval. Baseline and adjusted models were fit in a sample of 1,580,629 offspring. See eSupplement A for information about offspring who could be informative in sibling comparisons. Baseline models controlled for parity and year of birth. Adjusted models controlled parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts. Sibling comparisons controlled for parity and year of birth, paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts, and maternal age at childbearing.

Table 3. Adjusted associations between maternal antidepressant dispensations before pregnancy and during the first trimester of pregnancy and birth and neurodevelopmental outcomes

	Before pregnancy		1st trimester	
Any antidepressant				
	OR	**95% CI**	**OR**	**95% CI**
Preterm birth	1.17	1.07-1.28	1.40	1.33-1.47
Small for gestational age	1.07	0.93-1.24	1.12	1.03-1.21
	HR	**95% CI**	**HR**	**95% CI**
Autism spectrum disorder	1.40	1.02-1.93	1.75	1.49-2.07
Attention-deficit/hyperactivity disorder	2.09	1.53-2.86	1.85	1.55-2.20
SSRIs				
	OR	**95% CI**	**OR**	**95% CI**
Preterm birth	1.13	1.02-1.25	1.37	1.30-1.45
Small for gestational age	1.09	0.94-1.28	1.13	1.03-1.23
	HR	**95% CI**	**HR**	**95% CI**
Autism spectrum disorder	1.49	1.06-2.10	1.72	1.43-2.06
Attention-deficit/hyperactivity disorder	1.93	1.35-2.74	1.81	1.50-2.19

OR = odds ratio. HR = hazard ratio. CI = confidence interval. All models were fit in a sample of 708,450 offspring. Models controlled parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts.

Table 4. Baseline associations between paternal first-trimester antidepressant dispensations and birth and neurodevelopmental outcomes

	Any Antidepressant		SSRIs	
	OR	**95% CI**	**OR**	**95% CI**
Preterm birth	1.13	1.05-1.20	1.13	1.05-1.22
Small for gestational age	1.06	0.96-1.17	1.00	0.89-1.13
	HR	**95% CI**	**HR**	**95% CI**
Autism spectrum disorder	1.31	1.05-1.62	1.27	0.98-1.65
Attention-deficit/hyperactivity disorder	1.73	1.38-2.17	1.71	1.31-2.23

OR = odds ratio. HR = hazard ratio. CI = confidence interval. All models were fit in a sample of 708,450 offspring. Models controlled for parity and year of birth. Analyses compared offspring of fathers with first trimester antidepressant dispensations to offspring of fathers who were not dispensed antidepressants before pregnancy, during the second and third trimester of pregnancy, and after pregnancy (eFigure 1 shows dispensation windows).

Supplementary Online Content

eSupplement A:
Descriptive Statistics Based on Maternal Self-reported Antidepressant Use

In the main paper, we presented the distribution of covariates and outcomes stratified by maternal self-reported use of any antidepressant (Table 1). We have also provided the distribution of outcomes and covariates stratified by maternal self-reported use of any antidepressant in a subsample of differentially exposed siblings (eTable 1), as well as the distribution of outcomes and covariates stratified by maternal self-reported use of SSRIs specifically in all offspring in the sample and in a subsample of differentially exposed siblings (eTables 2 and 3, respectively). Because families in which all siblings are concordant on the outcomes cannot contribute to sibling comparison analyses, we have also provided information about subsamples of offspring from families with outcome-discordant siblings (eTable 4).

eTable 1. Descriptive statistics stratified by maternal self-reported first-trimester use of any antidepressant in a subsample of differentially exposed siblings

	Exposed offspring (n=10,975)	Unexposed offspring (n=13,994)
	No. (%)	**No. (%)**
Offspring outcomes		
Preterm birth	685 (6.24)	710 (5.07)
Small for gestational age	205 (1.87)	277 (1.98)
Autism spectrum disorder[a]	136 (5.52)	274 (4.55)
Attention-deficit/hyperactivity disorder[a]	280 (12.38)	699 (12.73)
Pregnancy covariates		
First born	2942 (26.81)	5803 (41.47)
Second born	4279 (38.99)	5346 (38.20)
Third born	2506 (22.83)	1803 (12.88)
Fourth born or higher	1248 (11.37)	1042 (7.45)
Born 1996 to 1999[b]	534 (4.87)	2648 (18.92)
Born 2000 to 2003[b]	1592 (14.51)	3653 (26.10)
Born 2004 to 2007[b]	3658 (33.33)	3882 (27.74)
Born 2008 to 2012[b]	5191 (47.30)	3811 (27.23)
Maternal covariates		
Age at birth		
< 20 years	111 (1.01)	509 (3.64)
20 to 24 years	1203 (10.96)	3158 (22.57)
25 to 29 years	3061 (27.89)	4720 (33.73)
30 to 34 years	3853 (35.11)	3800 (27.15)
35 to 39 years	2290 (20.87)	1543 (11.03)
≥ 40 years	457 (4.16)	264 (1.89)
Education		
Primary and lower secondary, < 9 years	99 (0.90)	141 (1.01)
Primary and lower secondary, 9 years	1375 (12.53)	1892 (13.52)
Upper secondary, 1-2 years	1951 (17.78)	2607 (18.63)
Upper secondary, 3 years	3022 (27.54)	3850 (27.51)
Post-secondary, < 3 years	1363 (12.42)	1670 (11.93)
Post-secondary, ≥ 3 years	3077 (28.04)	3737 (26.70)
Postgraduate	88 (0.80)	97 (0.69)
Nationality (Swedish)	9856 (89.80)	12469 (89.10)
Criminal convictions (any)	2007 (18.29)	2722 (19.45)
Severe psychiatric problem[c]	812 (7.40)	991 (7.08)
Suicide attempt (definite or uncertain)	1552 (14.14)	2018 (14.42)
Paternal covariates		
Age at birth		
< 20 years	50 (0.46)	191 (1.36)
20 to 24 years	706 (6.43)	1760 (12.58)
25 to 29 years	2358 (21.49)	4192 (29.96)
30 to 34 years	3571 (32.54)	4241 (30.31)
35 to 39 years	2666 (24.29)	2374 (16.96)
≥ 40 years	1624 (14.80)	1236 (8.83)
Education		
Primary and lower secondary, < 9 years	137 (1.25)	180 (1.29)

	Exposed offspring (n=10,975)	Unexposed offspring (n=13,994)
	No. (%)	**No. (%)**
Primary and lower secondary, 9 years	1290 (11.75)	1769 (12.64)
Upper secondary, 1-2 years	2810 (25.60)	3748 (26.78)
Upper secondary, 3 years	3076 (28.03)	3872 (27.67)
Post-secondary, < 3 years	1422 (12.96)	1788 (12.78)
Post-secondary, ≥ 3 years	2061 (18.78)	2420 (17.29)
Postgraduate	179 (1.63)	217 (1.55)
Nationality (Swedish)	9533 (86.86)	12023 (85.92)
Criminal convictions (any)	4603 (41.94)	6206 (44.35)
Severe psychiatric problem[c]	152 (1.38)	175 (1.25)
Suicide attempt (definite or uncertain)	621 (5.66)	802 (5.73)

All percentages are based on the number of offspring. [a]Age 15 Kaplan Meier estimates. [b]Year of birth is presented in bins in eTable 1 but was not binned when used as a covariate in models. [c]Severe psychiatric problem was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 2. Descriptive statistics stratified by maternal self-reported first-trimester SSRI use

	Exposed offspring (n=18,470)	Unexposed offspring (n=1,562,159)
	No. (%)	**No. (%)**
Offspring outcomes		
Preterm birth	1214 (6.57)	74847 (4.79)
Small for gestational age	453 (2.45)	34275 (2.19)
Autism spectrum disorder[a]	236 (5.21)	14381 (2.14)
Attention-deficit/hyperactivity disorder[a]	476 (13.29)	32448 (5.47)
Pregnancy covariates		
First born	8658 (46.88)	684412 (43.81)
Second born	5717 (30.95)	579902 (37.12)
Third born	2777 (15.04)	210605 (13.48)
Fourth born or higher	1318 (7.14)	87240 (5.58)
Born 1996 to 1999[b]	1063 (5.76)	332728 (21.30)
Born 2000 to 2003[b]	2340 (12.67)	346803 (22.20)
Born 2004 to 2007[b]	5230 (28.32)	381281 (24.41)
Born 2008 to 2012[b]	9837 (53.26)	501347 (32.09)
Maternal covariates		
Age at birth		
< 20 years	290 (1.57)	25347 (1.62)
20 to 24 years	2224 (12.04)	208328 (13.34)
25 to 29 years	5123 (27.74)	489927 (31.36)
30 to 34 years	6146 (33.28)	538600 (34.48)
35 to 39 years	3794 (20.54)	250977 (16.07)
≥ 40 years	893 (4.83)	48980 (3.14)
Education		
Primary and lower secondary, < 9 years	133 (0.72)	33515 (2.15)
Primary and lower secondary, 9 years	2115 (11.45)	105838 (6.78)
Upper secondary, 1-2 years	3009 (16.29)	243406 (15.58)
Upper secondary, 3 years	5043 (27.30)	409906 (26.24)
Post-secondary, < 3 years	2450 (13.26)	222256 (14.23)
Post-secondary, ≥ 3 years	5588 (30.25)	528122 (33.81)
Postgraduate	132 (0.71)	19116 (1.22)
Nationality (Swedish)	16719 (90.52)	1264423 (80.94)
Criminal convictions (any)	3158 (17.10)	170473 (10.91)
Severe psychiatric problem[c]	1350 (7.31)	15386 (0.98)
Suicide attempt (definite or uncertain)	2530 (13.70)	64125 (4.10)
Paternal covariates		
Age at birth		
< 20 years	116 (0.63)	7673 (0.49)
20 to 24 years	1287 (6.97)	99052 (6.34)
25 to 29 years	3973 (21.51)	361019 (23.11)
30 to 34 years	5890 (31.89)	541773 (34.68)
35 to 39 years	4371 (23.67)	350929 (22.46)
≥ 40 years	2833 (15.34)	201713 (12.91)
Education		
Primary and lower secondary, < 9 years	194 (1.05)	29175 (1.87)

	Exposed offspring (n=18,470)	Unexposed offspring (n=1,562,159)
	No. (%)	**No. (%)**
Primary and lower secondary, 9 years	2141 (11.59)	151436 (9.69)
Upper secondary, 1-2 years	4460 (24.15)	399459 (25.57)
Upper secondary, 3 years	5261 (28.48)	376485 (24.10)
Post-secondary, < 3 years	2408 (13.04)	231152 (14.80)
Post-secondary, ≥ 3 years	3697 (20.02)	344700 (22.07)
Postgraduate	309 (1.67)	29752 (1.90)
Nationality (Swedish)	16195 (87.68)	1257778 (80.52)
Criminal convictions (any)	7538 (40.81)	574464 (36.77)
Severe psychiatric problem[c]	247 (1.34)	10126 (0.65)
Suicide attempt (definite or uncertain)	1082 (5.86)	63797 (4.08)

All percentages are based on the number of offspring. [a]Age 15 Kaplan Meier estimates. [b]Year of birth is presented in bins in eTable 2 but was not binned when used as a covariate in models. [c]Severe psychiatric problem was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 3. Descriptive statistics stratified by maternal self-reported first-trimester use of SSRIs in a subsample of differentially exposed siblings

	Exposed offspring (n=9,063)	Unexposed offspring (n=15,906)
	No. (%)	**No. (%)**
Offspring outcomes		
Preterm birth	544 (6.00)	851 (5.35)
Small for gestational age	162 (1.79)	320 (2.01)
Autism spectrum disorder[a]	108 (5.59)	229 (4.64)
Attention-deficit/hyperactivity disorder[a]	229 (13.61)	585 (13.00)
Pregnancy covariates		
First born	2377 (26.23)	6368 (40.04)
Second born	3639 (40.15)	5986 (37.63)
Third born	2072 (22.86)	2237 (14.06)
Fourth born or higher	975 (10.76)	1315 (8.27)
Born 1996 to 1999[b]	369 (4.07)	2813 (17.69)
Born 2000 to 2003[b]	1256 (13.86)	3989 (25.08)
Born 2004 to 2007[b]	3027 (33.40)	4513 (28.37)
Born 2008 to 2012[b]	4411 (48.67)	4591 (28.86)
Maternal covariates		
Age at birth		
< 20 years	96 (1.06)	524 (3.29)
20 to 24 years	1003 (11.07)	3358 (21.11)
25 to 29 years	2554 (28.18)	5227 (32.86)
30 to 34 years	3146 (34.71)	4507 (28.34)
35 to 39 years	1888 (20.83)	1945 (12.23)
≥ 40 years	376 (4.15)	345 (2.17)
Education		
Primary and lower secondary, < 9 years	83 (0.92)	157 (0.99)
Primary and lower secondary, 9 years	1075 (11.86)	2192 (13.78)
Upper secondary, 1-2 years	1555 (17.16)	3003 (18.88)
Upper secondary, 3 years	2548 (28.11)	4324 (27.18)
Post-secondary, < 3 years	1118 (12.34)	1915 (12.04)
Post-secondary, ≥ 3 years	2614 (28.84)	4200 (26.41)
Postgraduate	70 (0.77)	115 (0.72)
Nationality (Swedish)	8157 (90.00)	14168 (89.07)
Criminal convictions (any)	1607 (17.73)	3122 (19.63)
Severe psychiatric problem[c]	630 (6.95)	1173 (7.37)
Suicide attempt (definite or uncertain)	1203 (13.27)	2367 (14.88)
Paternal covariates		
Age at birth		
< 20 years	42 (0.46)	199 (1.25)
20 to 24 years	580 (6.40)	1886 (11.86)
25 to 29 years	1933 (21.33)	4617 (29.03)
30 to 34 years	2989 (32.98)	4823 (30.32)
35 to 39 years	2189 (24.15)	2851 (17.92)
≥ 40 years	1330 (14.68)	1530 (9.62)
Education		
Primary and lower secondary, < 9 years	108 (1.19)	209 (1.31)

	Exposed offspring (n=9,063)	Unexposed offspring (n=15,906)
	No. (%)	**No. (%)**
Primary and lower secondary, 9 years	1054 (11.63)	2005 (12.61)
Upper secondary, 1-2 years	2283 (25.19)	4275 (26.88)
Upper secondary, 3 years	2557 (28.21)	4391 (27.61)
Post-secondary, < 3 years	1180 (13.02)	2030 (12.76)
Post-secondary, ≥ 3 years	1727 (19.06)	2754 (17.31)
Postgraduate	154 (1.70)	242 (1.52)
Nationality (Swedish)	7898 (87.15)	13658 (85.87)
Criminal convictions (any)	3771 (41.61)	7038 (44.25)
Severe psychiatric problem[c]	122 (1.35)	205 (1.29)
Suicide attempt (definite or uncertain)	499 (5.51)	924 (5.81)

All percentages are based on the number of offspring. [a]Age 15 Kaplan Meier estimates. [b]Year of birth is presented in bins in eTable 3 but was not binned when used as a covariate in models. [c]Severe psychiatric problem was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 4. Information on families with outcome discordant siblings in the cohort born 1996 to 2012

	Number of distinct outcome discordant siblings	Number of distinct mothers with outcome discordant offspring	Number of siblings with outcomes
Preterm birth	96866	40416	42557
Small for gestational age	45155	18926	19581
Autism spectrum disorder	24969	10105	10371
Attention-deficit/hyperactivity disorder	55526	22301	23522

eSupplement B:
Descriptive Statistics and Analyses Based on Antidepressant Dispensation Records

Exposure status was based on dispensation data for the timing of exposure comparisons and paternal comparisons. Dispensation windows used in main analyses were: (1) only before pregnancy, (2) during the first trimester of pregnancy, (3) only during the second and/or third trimester, and (4) only after pregnancy (see eFigure 1 for a diagram of the dispensation windows). We have presented the distribution of outcomes and covariates stratified by maternal dispensation windows for any antidepressants and for SSRIs specifically (eTables 5 and 6, respectively). In addition, we have presented the distribution of outcomes and covariates for offspring of fathers with first-trimester dispensations and offspring of fathers without dispensations before, during, or after pregnancy (see eTable 7 for any antidepressant dispensations and eTable 8 for SSRI dispensations).

Timing of exposure analyses compared associations with dispensations before pregnancy to associations with first-trimester dispensations. We evaluated whether these associations differed statistically using Wald χ^2 tests. We also compared the fit of two models using the Akaike information criterion (AIC). The first model included four parameters that compared the following groups to offspring unexposed to any antidepressants: (1) dispensations only before pregnancy, (2) dispensations for the first trimester of pregnancy, (3) dispensations only for the second and/or third trimester of pregnancy, and (4) dispensations only after pregnancy. The second model constrained the first two parameters to be equal so that the model included the following three parameters: (1) dispensations before and/or during the first trimester of pregnancy, (2) dispensations for the second and/or third trimester of pregnancy, and (3) dispensations after pregnancy. Thus, the four-parameter model included separate parameters for dispensations before pregnancy and first-trimester dispensations, whereas the three-parameter model included one parameter for dispensations before pregnancy and first-trimester dispensations. If associations with dispensations before pregnancy differed from associations with dispensations during the first trimester of pregnancy, the model that included separate parameters for those two time periods would fit better.

For preterm birth, the association between dispensations before pregnancy and preterm birth was significantly smaller than the association between first-trimester dispensations and preterm birth ($p = 0.0007$ for any antidepressant, $p = 0.001$ for SSRIs specifically), and the four-parameter model fit better than the three-parameter model. However, for small for gestational age, autism spectrum disorder, and attention-deficit/hyperactivity disorder the associations with dispensations before pregnancy did not significantly differ from associations with first-trimester dispensations (small for gestational age: $p = 0.64$ for any antidepressant, $p = 0.74$ for SSRIs specifically; autism spectrum disorder: $p = 0.21$ for any antidepressant, $p = 0.46$ for SSRIs specifically; attention-deficit/hyperactivity disorder: $p = 0.49$ for any antidepressant, $p = 0.76$ for SSRIs specifically). The three-parameter model also fit better than the four-parameter model for these outcomes. The four-parameter model estimates and the model fit for both models are presented in eTable 9.

eTable 5. Descriptive statistics stratified by maternal dispensation windows for any antidepressants

	Before pregnancy dispensations only (n=8203 [1.16%])	**1st-trimester dispensations** (n=26477 [3.74%])	**2nd and/or 3rd trimester dispensations only** (n=746 [0.11%])	**After pregnancy dispensations only** (n=6574 [0.93%])	**No dispensations before, during, or after pregnancy** (n=666450)
	No. (%)	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**
Offspring outcomes					
Preterm birth	484 (5.90)	1842 (6.96)	42 (5.63)	419 (6.37)	30945 (4.64)
Small for gestational age	205 (2.50)	660 (2.49)	20 (2.68)	148 (2.25)	14348 (2.15)
Autism spectrum disorder[a]	35 (0.96)	143 (1.14)	6 (2.00)	29 (0.90)	2044 (0.59)
Attention-deficit/hyperactivity disorder[a]	27 (1.03)	80 (0.83)	0 (0.00)	24 (0.88)	931 (0.34)
Pregnancy covariates					
First born	4097 (49.95)	12244 (46.24)	281 (37.67)	2666 (40.55)	296400 (44.47)
Second born	2298 (28.01)	8224 (31.06)	261 (34.99)	2586 (39.34)	250549 (37.59)
Third born	1219 (14.86)	4031 (15.22)	130 (17.43)	898 (13.66)	85821 912.88)
Fourth born or higher	589 (7.18)	1978 (7.47)	74 (9.92)	424 (6.45)	33680 (5.05)
Born 2006 to 2009[b]	4316 (52.61)	13570 (51.25)	364 (48.79)	3514 (53.45)	377773 (56.68)
Born 2010 to 2012[b]	3887 (47.39)	12907 (48.75)	382 (51.21)	3060 (46.55)	288677 (43.32)
Maternal covariates					
Age at birth					
< 20 years	152 (1.85)	439 (1.66)	20 (2.68)	172 (2.62)	9470 (1.42)
20 to 24 years	1244 (15.17)	3345 (12.63)	134 (17.96)	1080 (16.43)	84356 (12.66)
25 to 29 years	2257 (27.51)	7030 (26.55)	211 (28.28)	1871 (28.46)	193442 (29.03)
30 to 34 years	2660 (32.43)	8710 (32.90)	203 (27.21)	2080 (31.64)	234498 (35.19)
35 to 39 years	1522 (18.55)	5549 (20.96)	133 (17.83)	1088 (16.55)	120041 (18.01)
≥ 40 years	368 (4.49)	1404 (5.30)	45 (6.03)	283 (4.30)	24643 (3.70)
Education					
Primary and lower secondary, < 9 years	152 (1.85)	346 (1.31)	28 (3.75)	108 (1.64)	17093 (2.56)
Primary and lower secondary, 9 years	1077 (13.13)	3482 (13.15)	138 (18.58)	941 (14.31)	44637 (6.70)
Upper secondary, 1-2 years	1103 (13.45)	3513 (13.27)	97 (13.00)	820 (12.47)	61107 (9.17)
Upper secondary, 3 years	2363 (28.81)	7534 (28.45)	186 (24.93)	1922 (29.24)	189191 (28.39)
Post-secondary, < 3 years	1030 (12.56)	3358 (12.68)	104 (13.94)	789 (12.00)	84692 (12.71)
Post-secondary, ≥ 3 years	2408 (29.36)	8045 (30.38)	189 (25.34)	1956 (29.75)	261200 (39.19)
Postgraduate	70 (0.85)	199 (0.75)	4 (0.54)	38 (0.58)	8530 (1.28)

	Before pregnancy dispensations only (n=8203 [1.16%])	**1st-trimester dispensations** (n=26477 [3.74%])	**2nd and/or 3rd trimester dispensations only** (n=746 [0.11%])	**After pregnancy dispensations only** (n=6574 [0.93%])	**No dispensations before, during, or after pregnancy** (n=66450)
	No. (%)	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**
Nationality (Swedish)	6839 (83.37)	23220 (87.70)	543 (72.79)	5481 (83.37)	523334 (78.53)
Criminal convictions (any)	1417 (17.27)	4676 (17.66)	158 (21.18)	1058 (16.09)	62678 (9.40)
Severe psychiatric problem[c]	336 (4.10)	1736 (6.56)	37 (4.96)	370 (5.63)	3604 (0.54)
Suicide attempt (definite or uncertain)	1003 (12.23)	3685 (13.92)	101 (13.54)	676 (10.28)	23861 (3.58)
Paternal covariates					
Age at birth					
< 20 years	55 (0.67)	185 (0.70)	11 (1.47)	50 (0.76)	3033 (0.46)
20 to 24 years	708 (8.63)	2006 (7.58)	73 (9.79)	599 (9.11)	39498 (5.93)
25 to 29 years	1801 (21.96)	5543 (20.94)	165 (22.12)	1461 (22.22)	139335 (20.91)
30 to 34 years	2464 (30.04)	8096 (30.58)	200 (26.81)	2101 (31.96)	226642 (34.01)
35 to 39 years	1897 (23.13)	6260 (23.64)	176 (23.59)	1472 (22.39)	161388 (24.22)
≥ 40 years	1278 (15.58)	4387 (16.57)	121 (16.22)	891 (13.55)	96554 (14.49)
Education					
Primary and lower secondary, < 9 years	165 (2.01)	398 (1.50)	21 (2.82)	131 (1.99)	14251 (2.14)
Primary and lower secondary, 9 years	1027 (12.52)	3200 (12.09)	96 (12.87)	799 (12.15)	59882 (8.99)
Upper secondary, 1-2 years	1569 (19.13)	5345 (20.19)	150 (20.11)	1234 (18.77)	111799 (16.78)
Upper secondary, 3 years	2569 (31.32)	8243 (31.13)	224 (30.03)	2189 (33.30)	200790 (30.13)
Post-secondary, < 3 years	1052 (12.82)	3394 (12.82)	101 (13.54)	827 (12.58)	94032 (14.11)
Post-secondary, ≥ 3 years	1740 (21.21)	5536 (20.91)	143 (19.17)	1315 (20.00)	173513 (26.04)
Postgraduate	81 (0.99)	361 (1.36)	11 (1.47)	79 (1.20)	12183 (1.83)
Nationality (Swedish)	6704 (81.73)	22443 (84.76)	535 (71.72)	5415 (82.37)	522698 (78.43)
Criminal convictions (any)	3263 (39.78)	10434 (39.41)	309 (41.42)	2516 (38.27)	213431 (32.03)
Severe psychiatric problem[c]	78 (0.95)	351 (1.33)	8 (1.07)	88 (1.34)	3177 (0.48)
Suicide attempt (definite or uncertain)	488 (5.95)	1560 (5.89)	46 (6.17)	343 (5.22)	25464 (3.82)

All percentages are based on the number of offspring. [a]Age 6 Kaplan Meier estimates. [b]Year of birth is presented in bins in eTable 5 but was not binned when used as a covariate in models. [c]Severe psychiatric problem was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 6. Descriptive statistics stratified by maternal dispensation windows for SSRIs

	Before pregnancy dispensations (n=6674 [0.94%])	**1st-trimester dispensations** (n=22125 [3.12%])	**2nd/3rd trimester dispensations** (n=775 [0.11%])	**After pregnancy dispensations** (n=6007 [0.85%])	**No dispensations before, during, or after pregnancy** (n=672869)
	No. (%)	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**
Offspring outcomes					
Preterm birth	381 (5.71)	1512 (6.83)	41 (5.29)	378 (6.29)	31420 (4.67)
Small for gestational age	167 (2.50)	550 (2.49)	21 (2.71)	130 (2.16)	14513 (2.16)
Autism spectrum disorder[a]	30 (1.05)	115 (1.10)	6 (1.89)	31 (1.04)	2075 (0.59)
Attention-deficit/hyperactivity disorder[a]	21 (0.98)	64 (0.79)	1 (0.38)	24 (0.96)	952 (0.35)
Pregnancy covariates					
First born	3294 (49.36)	10220 (46.19)	293 (37.81)	2471 (41.14)	299410 (44.50)
Second born	1928 (28.89)	7022 (31.74)	274 (35.25)	2370 (39.45)	252324 (37.50)
Third born	997 (14.94)	3325 (15.03)	130 (16.77)	803 (13.37)	86844 (12.91)
Fourth born or higher	455 (6.82)	1558 (7.04)	78 (10.06)	363 (6.04)	34291 (5.10)
Born 2006 to 2009[b]	3550 (53.19)	11212 (50.68)	374 (48.26)	3192 (53.14)	381209 (56.65)
Born 2010 to 2012[b]	3124 (46.81)	10913 (49.32)	401 (51.74)	2815 (46.86)	291660 (43.35)
Maternal covariates					
Age at birth					
< 20 years	141 (2.11)	387 (1.75)	20 (2.58)	153 (2.55)	9552 (1.42)
20 to 24 years	1021 (15.30)	2826 (12.77)	140 (18.06)	1000 (16.65)	85172 (12.66)
25 to 29 years	1855 (27.79)	5926 (26.78)	218 (28.13)	1694 (28.20)	195118 (29.00)
30 to 34 years	2158 (32.33)	7269 (32.85)	216 (27.87)	1889 (31.45)	236619 (35.17)
35 to 39 years	1214 (18.19)	4580 (20.70)	137 (17.68)	1019 (16.96)	121383 (18.04)
≥ 40 years	285 (4.27)	1137 (5.14)	44 (5.68)	252 (4.20)	25025 (3.72)
Education					
Primary and lower secondary, < 9 years	108 (1.62)	254 (1.15)	29 (3.74)	90 (1.50)	17246 (2.56)
Primary and lower secondary, 9 years	880 (13.19)	2795 (12.63)	149 (19.23)	831 (13.83)	45620 (6.78)
Upper secondary, 1-2 years	857 (12.84)	2802 (12.66)	104 (13.42)	740 (12.32)	62137 (9.23)
Upper secondary, 3 years	1901 (28.48)	6303 (28.49)	194 (25.03)	1756 (29.23)	191042 (28.39)
Post-secondary, < 3 years	861 (12.90)	2831 (12.80)	109 (14.06)	730 (12.15)	85442 (12.70)
Post-secondary, ≥ 3 years	2012 (30.15)	6973 (31.52)	185 (23.87)	1824 (30.36)	262804 (39.06)
Postgraduate	55 (0.82)	167 (0.75)	5 (0.65)	36 (0.60)	8578 (1.27)

	Before pregnancy dispensations (n=6674 [0.94%])	**1st-trimester dispensations** (n=22125 [3.12%])	**2nd/3rd trimester dispensations** (n=775 [0.11%])	**After pregnancy dispensations** (n=6007 [0.85%])	**No dispensations before, during, or after pregnancy** (n=672869)
	No. (%)	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**
Nationality (Swedish)	5616 (84.15)	19486 (88.07)	570 (73.55)	5036 (83.84)	528709 (78.58)
Criminal convictions (any)	1160 (17.38)	3750 (16.95)	165 (21.29)	974 (16.21)	63938 (9.50)
Severe psychiatric problem[c]	278 (4.17)	1418 (6.41)	49 (6.32)	358 (5.96)	3980 (0.59)
Suicide attempt (definite or uncertain)	817 (12.24)	2927 (13.23)	112 (14.45)	625 (10.40)	24845 (3.69)
Paternal covariates					
Age at birth					
< 20 years	46 (0.69)	154 (0.70)	12 (1.55)	47 (0.78)	3075 (0.46)
20 to 24 years	608 (9.11)	1682 (7.60)	76 (9.81)	551 (9.17)	39967 (5.94)
25 to 29 years	1441 (21.59)	4662 (21.07)	169 (21.81)	1341 (22.32)	140692 (20.91)
30 to 34 years	2054 (30.78)	6823 (30.84)	216 (27.87)	1889 (31.45)	228521 (33.96)
35 to 39 years	1522 (22.80)	5248 (23.72)	175 (22.58)	1353 (22.52)	162895 (24.21)
≥ 40 years	1003 (15.03)	3556 (16.07)	127 (16.39)	826 (13.75)	97719 (14.52)
Education					
Primary and lower secondary, < 9 years	126 (1.89)	305 (1.38)	22 (2.84)	115 (1.91)	14398 (2.14)
Primary and lower secondary, 9 years	847 (12.69)	2612 (11.81)	108 (13.94)	724 (12.05)	60713 (9.02)
Upper secondary, 1-2 years	1241 (18.59)	4347 (19.65)	158 (20.39)	1110 (18.48)	113241 (16.83)
Upper secondary, 3 years	2076 (31.11)	6938 (31.36)	236 (30.45)	1996 (33.23)	202769 (30.13)
Post-secondary, < 3 years	864 (12.95)	2880 (13.02)	100 (12.90)	759 (12.64)	94803 (14.09)
Post-secondary, ≥ 3 years	1452 (21.76)	4731 (21.38)	139 (17.94)	1227 (20.43)	174698 (25.96)
Postgraduate	68 (1.02)	312 (1.41)	12 (1.55)	76 (1.27)	12247 (1.82)
Nationality (Swedish)	5491 (82.27)	18855 (85.22)	559 (72.13)	4960 (82.57)	527930 (78.46)
Criminal convictions (any)	2614 (39.17)	8608 (38.91)	333 (42.97)	2285 (38.04)	216113 (32.12)
Severe psychiatric problem[c]	74 (1.11)	289 (1.31)	8 (1.03)	87 (1.45)	3244 (0.48)
Suicide attempt (definite or uncertain)	416 (6.23)	1282 (5.79)	56 (7.23)	312 (5.19)	25835 (3.84)

All percentages are based on the number of offspring. [a]Age 6 Kaplan Meier estimates. [b]Year of birth is presented in bins in eTable 6 but was not binned when used as a covariate in models. [c]Severe psychiatric problem was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 7. Descriptive statistics stratified by paternal first-trimester dispensations of any antidepressants

	1st-trimester dispensations (n=18,727)	No dispensations before, during, or after pregnancy (n= 675,620)
	No. (%)	**No. (%)**
Offspring outcomes		
Preterm birth	992 (5.30)	32024 (4.74)
Small for gestational age	423 (2.26)	14623 (2.16)
Autism spectrum disorder[a]	77 (0.81)	2125 (0.61)
Attention-deficit/hyperactivity disorder[a]	49 (0.68)	972 (0.36)
Pregnancy covariates		
First born	7893 (42.15)	301793 (44.67)
Second born	6554 (35.00)	252447 (37.37)
Third born	2833 (15.13)	87218 (12.91)
Fourth born or higher	1447 (7.73)	34162 (5.06)
Born 2006 to 2009[b]	10064 (53.74)	381620 (56.48)
Born 2010 to 2012[b]	8663 (46.26)	294000 (43.52)
Maternal covariates		
Age at birth		
< 20 years	309 (1.65)	9583 (1.42)
20 to 24 years	2195 (11.72)	85688 (12.68)
25 to 29 years	4955 (26.46)	195867 (28.99)
30 to 34 years	6373 (34.03)	237503 (35.15)
35 to 39 years	3971 (21.20)	121792 (18.03)
≥ 40 years	924 (4.93)	25187 (3.73)
Education		
Primary and lower secondary, < 9 years	600 (3.20)	16585 (2.45)
Primary and lower secondary, 9 years	1838 (9.81)	46592 (6.90)
Upper secondary, 1-2 years	2140 (11.43)	62703 (9.28)
Upper secondary, 3 years	5271 (28.15)	191879 (28.40)
Post-secondary, < 3 years	2305 (12.31)	85920 (12.72)
Post-secondary, ≥ 3 years	6374 (34.04)	263433 (38.99)
Postgraduate	199 (1.06)	8508 (1.26)
Nationality (Swedish)	14604 (77.98)	534445 (79.10)
Criminal convictions (any)	2586 (13.81)	65127 (9.64)
Severe psychiatric problem[c]	379 (2.02)	5393 (0.80)
Suicide attempt (definite or uncertain)	1192 (6.37)	27118 (4.01)
Paternal covariates		
Age at birth		
< 20 years	83 (0.44)	3158 (0.47)
20 to 24 years	844 (4.51)	40960 (6.06)
25 to 29 years	3099 (16.55)	142359 (21.07)
30 to 34 years	5746 (30.68)	229720 (34.00)
35 to 39 years	4980 (26.59)	162975 (24.12)
≥ 40 years	3975 (21.23)	96448 (14.28)
Education		
Primary and lower secondary, < 9 years	474 (2.53)	13993 (2.07)
Primary and lower secondary, 9 years	2640 (14.10)	59944 (8.87)

	1st-trimester dispensations (n=18,727)	No dispensations before, during, or after pregnancy (n= 675,620)
	No. (%)	**No. (%)**
Upper secondary, 1-2 years	3871 (20.67)	113159 (16.75)
Upper secondary, 3 years	4931 (26.33)	205399 (30.40)
Post-secondary, < 3 years	2347 (12.53)	95382 (14.12)
Post-secondary, ≥ 3 years	4156 (22.19)	175515 (25.98)
Postgraduate	308 (1.64)	12228 (1.81)
Nationality (Swedish)	14870 (79.40)	532719 (78.85)
Criminal convictions (any)	8514 (45.46)	214354 (31.73)
Severe psychiatric problem[c]	978 (5.22)	2142 (0.32)
Suicide attempt (definite or uncertain)	1808 (9.65)	24632 (3.65)

All percentages are based on the number of offspring. [a]Age 6 Kaplan Meier estimates. [b]Year of birth is presented in bins in eTable 7 but was not binned when used as a covariate in models. [c]Severe psychiatric problem was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 8. Descriptive statistics stratified by paternal first-trimester dispensations of SSRIs

	1st-trimester dispensations (n=13,521)	No dispensations before, during, or after pregnancy (n=684,714)
	No. (%)	**No. (%)**
Offspring outcomes		
Preterm birth	720 (5.33)	32486 (4.74)
Small for gestational age	291 (2.15)	14851 (2.17)
Autism spectrum disorder[a]	55 (0.75)	2157 (0.61)
Attention-deficit/hyperactivity disorder[a]	37 (0.67)	994 (0.36)
Pregnancy covariates		
First born	5754 (42.56)	305525 (44.62)
Second born	4776 (35.32)	255557 (37.32)
Third born	2032 (15.03)	88602 (12.94)
Fourth born or higher	959 (7.09)	35030 (5.12)
Born 2006 to 2009[b]	7252 (53.64)	386666 (56.47)
Born 2010 to 2012[b]	6269 (46.36)	298048 (43.53)
Maternal covariates		
Age at birth		
< 20 years	222 (1.64)	9756 (1.42)
20 to 24 years	1496 (11.06)	87065 (12.72)
25 to 29 years	3616 (26.74)	198353 (28.97)
30 to 34 years	4675 (34.58)	240266 (35.09)
35 to 39 years	2859 (21.14)	123621 (18.05)
≥ 40 years	653 (4.83)	25653 (3.75)
Education		
Primary and lower secondary, < 9 years	347 (2.57)	17032 (2.49)
Primary and lower secondary, 9 years	1216 (8.99)	47800 (6.98)
Upper secondary, 1-2 years	1471 (10.88)	63936 (9.34)
Upper secondary, 3 years	3816 (28.22)	194470 (28.40)
Post-secondary, < 3 years	1656 (12.25)	86992 (12.70)
Post-secondary, ≥ 3 years	4873 (36.04)	265887 (38.83)
Postgraduate	142 (1.05)	8597 (1.26)
Nationality (Swedish)	10890 (80.54)	540855 (78.99)
Criminal convictions (any)	1756 (12.99)	66667 (9.74)
Severe psychiatric problem[c]	248 (1.83)	5608 (0.82)
Suicide attempt (definite or uncertain)	839 (6.21)	27761 (4.05)
Paternal covariates		
Age at birth		
< 20 years	67 (0.50)	3201 (0.47)
20 to 24 years	608 (4.50)	41491 (6.06)
25 to 29 years	2300 (17.01)	143887 (21.01)
30 to 34 years	4284 (31.68)	232237 (33.92)
35 to 39 years	3649 (26.99)	165167 (24.12)
≥ 40 years	2613 (19.33)	98731 (14.42)
Education		
Primary and lower secondary, < 9 years	270 (2.00)	14374 (2.10)
Primary and lower secondary, 9 years	1764 (13.05)	61624 (9.00)
Upper secondary, 1-2 years	2705 (20.01)	115293 (16.84)

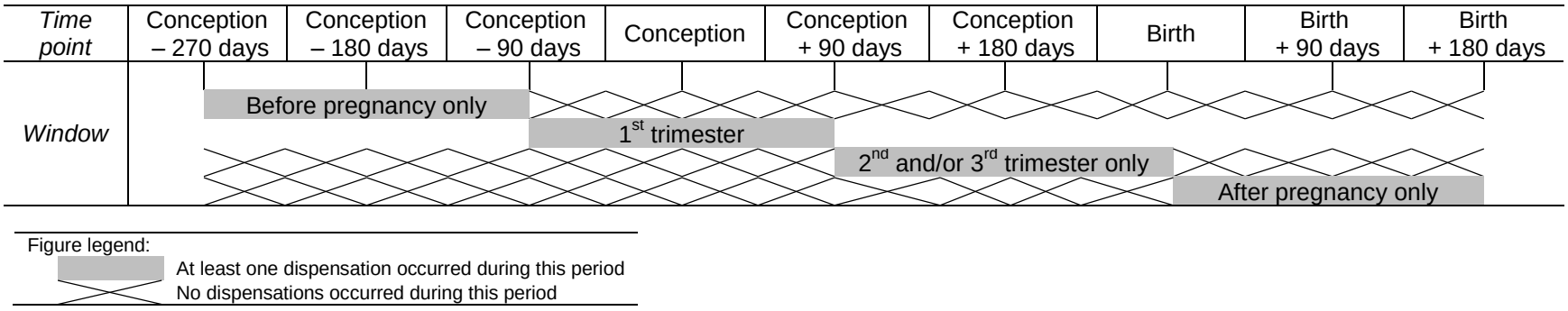
	1st-trimester dispensations (n=13,521)	**No dispensations before, during, or after pregnancy** (n=684,714)
	No. (%)	**No. (%)**
Upper secondary, 3 years	3658 (27.05)	207594 (30.32)
Post-secondary, < 3 years	1692 (12.51)	96471 (14.09)
Post-secondary, ≥ 3 years	3199 (23.66)	177024 (25.85)
Postgraduate	233 (1.72)	12334 (1.80)
Nationality (Swedish)	11062 (81.81)	539150 (78.74)
Criminal convictions (any)	5885 (43.52)	219182 (32.01)
Severe psychiatric problem[c]	620 (4.59)	2634 (0.38)
Suicide attempt (definite or uncertain)	1126 (8.33)	25773 (3.76)

All percentages are based on the number of offspring. [a]Age 6 Kaplan Meier estimates. [b]Year of birth is presented in bins in eTable 8 but was not binned when used as a covariate in models. [c]Severe psychiatric problem was defined as an inpatient or outpatient diagnosis of schizophrenia, bipolar disorder, or other non-drug induced psychosis.

eTable 9. Adjusted associations between maternal antidepressant dispensations before pregnancy, during the first trimester of pregnancy, during the second and/or third trimester of pregnancy, and after pregnancy and offspring birth and neurodevelopmental outcomes

	Four parameter model estimates								Model fit	
	1. Before pregnancy		2. 1st trimester		3. 2nd and/or 3rd trimester		4. After pregnancy		Four Parameter model	Parameters 1 and 2 constrained to equality
Any antidepressant										
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**AIC**	**AIC**
Preterm birth	1.17	1.07-1.28	1.40	1.33-1.47	1.15	0.84-1.57	1.34	1.21-1.48	268512.64	268522.38
Small for gestational age	1.07	0.93-1.24	1.12	1.03-1.21	1.17	0.75-1.84	1.05	0.89-1.24	143724.04	143722.26
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**	**AIC**	**AIC**
Autism spectrum disorder	1.40	1.02-1.93	1.75	1.49-2.07	2.18	0.98-4.85	1.45	1.03-2.04	65876.69	65876.32
Attention deficit/hyperactivity disorder	2.09	1.53-2.86	1.85	1.55-2.20	0.24	0.06-1.01	1.86	1.39-2.48	46856.51	46854.97
SSRIs										
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**AIC**	**AIC**
Preterm birth	1.13	1.02-1.25	1.37	1.30-1.45	1.06	0.77-1.45	1.31	1.18-1.46	268561.62	268570.72
Small for gestational age	1.09	0.94-1.28	1.13	1.03-1.23	1.17	0.76-1.82	1.01	0.85-1.21	143723.97	143722.08
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**	**AIC**	**AIC**
Autism spectrum disorder	1.49	1.06-2.10	1.72	1.43-2.06	2.13	0.96-4.76	1.64	1.17-2.29	65881.61	65880.16
Attention deficit/hyperactivity disorder	1.93	1.35-2.74	1.81	1.50-2.19	0.50	0.17-1.42	1.86	1.37-2.52	46876.16	46874.25

OR = odds ratio. HR = hazard ratio. CI = confidence interval. Models were fit in a sample of 708,450 offspring. The four parameter model included the following four parameters that compared the following groups to offspring unexposed to any antidepressants: (1) dispensations only before pregnancy, (2) dispensations for the first trimester of pregnancy, (3) dispensations only for the second and/or third trimester of pregnancy, and (4) dispensations only after pregnancy. Models also controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts. Models were compared using the Akaike information criterion (AIC).



eFigure 1. Dispensation windows. The before-pregnancy-only window included offspring of women who were dispensed antidepressants in the period 270 days before conception to 90 days before conception but were not dispensed antidepressants in the period 90 days before conception to 180 days after birth. The 1st-trimester window included offspring of women who were dispensed antidepressants in the period 90 days before conception to 90 days after conception. Offspring of women who were also dispensed antidepressants before or after the defined exposure window were considered exposed in the 1st-trimester window. The 2nd- and/or 3rd-trimester only window included offspring of women who were dispensed antidepressants in the period 90 days after conception to birth but were not dispensed antidepressants in the period 270 days before conception to 90 days after conception and were not dispensed antidepressants in the period 180 days after birth. The after pregnancy only window included offspring of women who were dispensed antidepressants in the period 180 days after birth but were not dispensed antidepressants in the period 270 days before conception through birth.

eSupplement C:
Test of Exposure Misclassification

In the sample of 708,450 offspring born between 2006 and 2012, maternal self-report data on antidepressant use was used in combination with maternal antidepressant dispensation data to evaluate whether exposure misclassification may have biased the results.

The main analyses used two different definitions for first-trimester antidepressant exposure. First-trimester exposure was defined (a) according to maternal self-reports and (b) according to dispensation data. Women self-reported antidepressant use at the first antenatal visit, which typically occur between the 10^{th} and 12^{th} week of pregnancy. First-trimester exposure based on dispensation records was defined as having at least one dispensation between 90 days before estimated conception and 90 days after estimated conception. (eFigure 1 shows a diagram of exposure windows.)

To test for biases from exposure misclassification, we first calculated kappa estimates to assess agreement between the two exposures definitions used in the main analyses.

Then, four additional exposure definitions were created.

The first definition classified cases as exposed if *either* exposure definition used in the main analyses indicated exposure. According to this definition, 28,158 (4.0% of the 2006-2012 cohort) offspring were exposed to any antidepressant, and 23,422 (3.3%) offspring were exposed to SSRIs specifically.

The second definition classified cases as exposed if *both* exposure definitions used in the main analyses indicated exposure. According to this definition, 13,435 (1.9%) offspring were exposed to any antidepressant, and 11,516 (1.6%) offspring were exposed to SSRIs specifically.

The third definition used a narrower window than the main analyses' first-trimester dispensation definition. Specifically, it defined exposure as having at least one dispensation between *30* days before estimated conception and 90 days after estimated conception. According to this definition, 7,455 (1.1%) offspring were exposed to any antidepressant, and 5,593 (0.8%) offspring were exposed to SSRIs specifically.

The fourth definition required at least *two* dispensations in the dispensation window used in the main analyses (between 90 days before estimated conception and 90 days after estimated conception). According to this definition, 14,288 (2.0%) offspring were exposed to any antidepressant, and 11,333 (1.6%) offspring were exposed to SSRIs specifically.

Models assessing associations between the four additional definitions of exposure and offspring problems included pregnancy-related, maternal, and paternal covariates.

In general, the results from the sensitivity analyses suggest that exposure misclassification and self-report biases did not influence the results.

Maternal reports and dispensation records showed substantial agreement (kappa = 0.64, 95% CI [0.63 to 0.64] for any antidepressant, and kappa = 0.65, 95% CI [0.65 to 0 .66] for SSRIs). Additionally, commensurate associations were found across the two exposure definitions used in the main paper and the four additional definitions described here (Table 2, Table 3, eTable 10).

eTable 10. Adjusted associations between four definitions of first-trimester antidepressant use and offspring birth and neurodevelopmental outcomes

	Exposure according to self-reported use *OR* dispensation data		Exposure according to self-report use *AND* dispensation data		Narrower first-trimester exposure dispensation window		Two dispensations during 1st trimester	
Any antidepressant								
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Preterm birth	1.38	1.31-1.45	1.40	1.31-1.50	1.44	1.36-1.52	1.54	1.41-1.68
Small for gestational age	1.12	1.03-1.21	1.13	1.01-1.26	1.14	1.04-1.25	1.13	0.98-1.31
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Autism spectrum disorder	1.71	1.46-2.01	1.83	1.46-2.28	1.85	1.54-2.22	1.72	1.28-2.31
Attention deficit/hyperactivity disorder	1.70	1.44-2.00	1.75	1.38-2.22	1.83	1.50-2.22	1.81	1.34-2.44
SSRIs								
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Preterm birth	1.34	1.27-1.42	1.34	1.24-1.44	1.42	1.34-1.51	1.45	1.31-1.61
Small for gestational age	1.12	1.03-1.22	1.13	1.01-1.28	1.17	1.06-1.29	1.17	0.99-1.38
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Autism spectrum disorder	1.71	1.44-2.04	1.75	1.37-2.24	1.83	1.50-2.24	1.71	1.21-2.41
Attention deficit/hyperactivity disorder	1.62	1.35-1.95	1.76	1.36-2.28	1.87	1.51-2.31	1.83	1.29-2.58

OR = odds ratio. HR = hazard ratio. CI = confidence interval. Models were fit in a sample of 708,450 offspring. Models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts.

eSupplement D:
Test of Generalizability of Sibling Comparisons

An assumption of sibling comparisons is that results will generalize to other samples (e.g., families with only one child, families without variability in the outcome). An additional analysis was conducted to test this assumption. Specifically, given that families with single included offspring were excluded from sibling comparison analyses (because they cannot provide information), we assessed baseline and adjusted associations in a subsample of 1,139,753 offspring who had at least one sibling in the dataset in order to assess the generalizability of the sibling comparison results. Although associations with small for gestational age were not statistically significant, the general pattern of results were consistent with findings from the main analyses (eTable 11), suggesting that reduction in the effect sizes in the sibling-comparison models, particularly for the neurodevelopmental outcomes, was not due to the exclusion of single-offspring families.

eTable 11. Baseline and adjusted associations between maternal self-reported first-trimester antidepressant use and offspring birth and neurodevelopmental outcomes in multiple-offspring families

	Baseline Model		Adjusted Model	
Any antidepressant				
	OR	**95% CI**	**OR**	**95% CI**
Preterm birth	1.48	1.38-1.58	1.37	1.28-1.47
Small for gestational age	1.06	0.94-1.20	1.06	0.94-1.19
	HR	**95% CI**	**HR**	**95% CI**
Autism spectrum disorder	2.08	1.80-2.39	1.70	1.47-1.96
Attention deficit/hyperactivity disorder	2.09	1.89-2.31	1.48	1.34-1.64
SSRIs				
	OR	**95% CI**	**OR**	**95% CI**
Preterm birth	1.39	1.29-1.50	1.29	1.20-1.39
Small for gestational age	1.03	0.90-1.18	1.03	0.90-1.18
	HR	**95% CI**	**HR**	**95% CI**
Autism spectrum disorder	2.06	1.75-2.42	1.69	1.44-1.99
Attention deficit/hyperactivity disorder	2.18	1.94-2.44	1.54	1.37-1.73

OR = odds ratio. HR = hazard ratio. CI = confidence interval. All models were fit in a sample of 1,139,753 offspring who had at least one sibling in the dataset. Baseline models controlled for parity and year of birth. Adjusted models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts.

eSupplement E:
Test of Confounding from Exposure to Other Psychotropic Medications

Offspring with maternal self-reported first-trimester exposure to other psychotropic medications, defined as antiepileptic medications, antipsychotic medications, medications used to treat addictive disorders, anxiolytics, attention-deficit/hyperactivity disorder medication, and opioid analgesics, were identified (eTable 12 lists specific drug names and Anatomical Therapeutic Chemical Classification [ATC] codes). Given that 9.8% (2,204) of offspring exposed to antidepressants were also exposed to other psychotropic medications, associations between maternal self-reported first-trimester antidepressant use and offspring outcomes were assessed in a subsample of 1,563,250 offspring who were not exposed to the other psychotropic medications. These associations were commensurate to associations observed in the main analyses (eTable 13), suggesting that exposure to other psychotropic medications did not bias the results.

eTable 12. Drug names and Anatomical Therapeutic Chemical Classification codes for other psychotropic medications

ATC code	Medication name
Antiepileptic medications	
N03AA01	methylphenobarbital
N03AA02	phenobarbital
N03AA03	primidone
N03AA04	barbexaclone
N03AA30	metharbital
N03AB01	ethotoin
N03AB02	phenytoin
N03AB03	amino(diphenylhydantoin) valeric acid
N03AB04	mephenytoin
N03AB05	fosphenytoin
N03AB52	phenytoin, combinations
N03AB54	mephenytoin, combinations
N03AC01	paramethadione
N03AC02	trimethadione
N03AC03	ethadione
N03AD01	ethosuximide
N03AD02	phensuximide
N03AD03	mesuximide
N03AD51	ethosuximide, combinations
N03AF01	carbamazepine
N03AF02	oxcarbazepine
N03AF03	rufinamide
N03AF04	eslicarbazepine
N03AG01	valproic acid
N03AG02	valpromide
N03AG03	aminobutyric acid
N03AG04	vigabatrin
N03AG05	progabide
N03AG06	tiagabine
N03AX03	sultiame
N03AX07	phenacemide
N03AX09	lamotrigine
N03AX10	felbamate
N03AX11	topiramate
N03AX12	gabapentin
N03AX13	pheneturide
N03AX14	levetiracetam
N03AX15	zonisamide
N03AX16	pregabalin

ATC code	Medication name
Antiepileptic medications	
N03AX17	stiripentol
N03AX18	lacosamide
N03AX19	carisbamate
N03AX21	retigabine
N03AX22	perampanel
N03AX30	beclamide
N05AN01	lithium
Antipsychotic medications	
N05AA01	chlorpromazine
N05AA02	levomepromazine
N05AA03	promazine
N05AA04	acepromazine
N05AA05	triflupromazine
N05AA06	cyamemazine
N05AA07	chlorproethazine
N05AB01	dixyrazine
N05AB02	fluphenazine
N05AB03	perphenazine
N05AB04	prochlorperazine
N05AB05	thiopropazate
N05AB06	trifluoperazine
N05AB07	acetophenazine
N05AB08	thioproperazine
N05AB09	butaperazine
N05AB10	perazine
N05AC01	periciazine
N05AC02	thioridazine
N05AC03	mesoridazine
N05AD01	haloperidol
N05AD02	trifluperidol
N05AD03	melperone
N05AD04	moperone
N05AD05	pipamperone
N05AD06	bromperidol
N05AD07	benperidol
N05AD08	droperidol
N05AD09	fluanisone
N05AE01	oxypertine
N05AE02	molindone
N05AE03	sertindole
N05AE04	ziprasidone

ATC code	Medication name
Antipsychotic medications	
N05AE05	lurasidone
N05AF01	flupentixol
N05AF02	clopenthixol
N05AF03	chlorprothixene
N05AF04	tiotixene
N05AF05	zuclopenthixol
N05AG01	fluspirilene
N05AG02	pimozide
N05AG03	penfluridol
N05AH01	loxapine
N05AH02	clozapine
N05AH03	olanzapine
N05AH04	quetiapine
N05AH05	asenapine
N05AH06	clotiapine
N05AL01	sulpiride
N05AL02	sultopride
N05AL03	tiapride
N05AL04	remoxipride
N05AL05	amisulpride
N05AL06	veralipride
N05AL07	levosulpiride
N05AX07	prothipendyl
N05AX08	risperidone
N05AX10	mosapramine
N05AX11	zotepine
N05AX12	aripiprazole
N05AX13	paliperidone
N05AX14	iloperidone
Medications for addictive disorders	
N07BA01	nicotine
N07BA03	varenicline
N07BB01	disulfiram
N07BB02	calcium carbimide
N07BB03	acamprosate
N07BB04	naltrexone
N07BC01	buprenorphine
N07BC02	methadone
N07BC03	levacetylmethadol
N07BC04	lofexidine
N07BC05	levomethadone

ATC code	Medication name
Medications for addictive disorders	
N07BC06	diamorphine
N07BC51	buprenorphine, combinations
Anxiolytics	
N03AE01	clonazepam
N05BA01	diazepam
N05BA02	chlordiazepoxide
N05BA04	oxazepam
N05BA05	clorazepate
N05BA06	lorazepam
N05BA12	alprazolam
N05CD01	flurazepam
N05CD04	estazolam
N05CD05	triazolam
N05CD07	temazepam
N05CD08	midazolam
N05CD1l0	quazepam
N05BE01	buspirone
N05BB01	atarax
N05BB01	vistaril
Attention-deficit/hyperactivity disorder medications	
N06BA01	amfetamine
N06BA02	dexamfetamine
N06BA04	methylphenidate
N06BA09	atomoxetine
Opioids	
N02AA01	Morphine
N02AA03	Hydromorphine
N02AA05	Oxycodone
N02AA55	Oxycodone/nalaxone
N02AA59	Codeine excl. psychotropics
N02AB01	Ketobemidone
N02AB02	Pethidine
N02AB03	Fentanyl
N02AC04	Dextropropoxyphene
N02AC54	Dextropropoxyphene excl psycholeptics
N02AD01	Pentazocine
N02AE01	Buprenorphine
N02AG01	Morphine & antispasmodics
N02AG02	Ketobemidone/ dimethylaminophenylbutene
N02AG04	Hydromorphone & antispasmodics

ATC code	Medication name
Opioids	
N02AX02	Tramadol

ATC = Anatomical Therapeutic Chemical Classification

eTable 13. Baseline, adjusted, and sibling comparison associations between maternal self-reported first-trimester antidepressant use and offspring birth and neurodevelopmental outcomes in a subsample of offspring *not exposed* to other psychotropic medications

	Baseline Model		Adjusted Model		Sibling Comparison	
Any antidepressant						
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Preterm birth	1.40	1.32-1.48	1.30	1.22-1.37	1.30	1.13-1.49
Small for gestational age	1.12	1.03-1.23	1.11	1.02-1.22	0.92	0.73-1.17
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Autism spectrum disorder	1.85	1.64-2.10	1.53	1.35-1.74	0.67	0.48-0.94
Attention deficit/hyperactivity disorder	2.16	1.99-2.35	1.58	1.46-1.72	1.02	0.79-1.30
SSRIs						
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Preterm birth	1.31	1.23-1.40	1.22	1.15-1.30	1.27	1.10-1.48
Small for gestational age	1.08	0.98-1.20	1.08	0.98-1.20	0.82	0.63-1.06
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Autism spectrum disorder	1.85	1.61-2.13	1.53	1.33-1.76	0.67	0.46-0.97
Attention deficit/hyperactivity disorder	2.17	1.98-2.39	1.58	1.44-1.74	0.96	0.73-1.27

OR = odds ratio. HR = hazard ratio. CI = confidence interval. Baseline and adjusted models were fit in a sample of 1,563,250 offspring. Baseline models controlled for parity and year of birth. Adjusted models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts. Sibling comparisons controlled for parity and year of birth, paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts, and maternal age at childbearing.

eSupplement F:
Test of Bias from Left Censoring

Given that, prior to 2001, outpatient psychiatric diagnoses were not included in the National Patient Register, we conducted analyses in a sample of 1,162,873 offspring born in 2001 or later to assess whether left censoring of the neurodevelopmental outcomes may have biased the results. The analyses also enabled us to examine whether cohort effects influenced the results. These analyses assessed associations between maternal self-reported first-trimester antidepressant use and offspring autism spectrum disorder and attention-deficit/hyperactivity disorder in baseline, adjusted, and sibling comparison models. The results were commensurate to the main analyses (eTable 14), suggesting that left censoring of the outcomes and cohort effects did not influence the results.

eTable 14. Baseline, adjusted, and sibling comparison associations between maternal self-reported first-trimester antidepressant use and offspring neurodevelopmental outcomes in a subsample born in 2001 or after

	Baseline Model		Adjusted Model		Sibling Comparison	
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Any antidepressant						
Autism spectrum disorder	2.04	1.79-2.32	1.71	1.49-1.95	0.88	0.59-1.33
Attention-deficit/hyperactivity disorder	2.29	2.09-2.52	1.63	1.48-1.80	1.05	0.73-1.50
SSRIs						
Autism spectrum disorder	2.06	1.78-2.38	1.75	1.51-2.02	0.90	0.58-1.40
Attention-deficit/hyperactivity disorder	2.28	2.05-2.53	1.63	1.46-1.81	0.92	0.62-1.35

HR = hazard ratio. CI = confidence interval. Baseline and adjusted models were fit in a sample of 1,162,873 offspring. Baseline models controlled for parity and year of birth. Adjusted models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts. Sibling comparisons controlled for parity and year of birth, paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts, and maternal age at childbearing.

eSupplement G:
Test of Validity of Early Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder Diagnoses

There is uncertainty about the stability over time of early neurodevelopmental disorder diagnoses.[e.g.,1] Thus, we conducted a sensitivity analyses to test the validity of early autism spectrum disorder and attention-deficit/hyperactivity disorder diagnoses. Offspring diagnosed before the age of 2 were excluded from the sample and baseline, adjusted, and sibling comparison associations were re-examined. Associations with autism spectrum disorder were assessed in a sample of 1,580,430 offspring. Associations with attention-deficit/hyperactivity disorder were assessed in a sample of 1,580,509 offspring. Associations were commensurate to main analyses associations (eTable 15), suggesting that early neurodevelopmental diagnoses of potentially questionable validity did not bias the results.

eTable 15. Baseline, adjusted, and sibling comparison associations between maternal self-reported first-trimester antidepressant use and offspring neurodevelopmental outcomes in a sample excluding offspring diagnosed before age 2 years

	Baseline Model		Adjusted Model		Sibling Comparison	
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Any antidepressant						
Autism spectrum disorder	2.01	1.80-2.26	1.63	1.45-1.83	0.83	0.61-1.13
Attention-deficit/hyperactivity disorder	2.21	2.04-2.38	1.58	1.46-1.71	1.00	0.79-1.26
SSRIs						
Autism spectrum disorder	2.03	1.79-2.31	1.65	1.45-1.88	0.81	0.57-1.14
Attention-deficit/hyperactivity disorder	2.25	2.06-2.46	1.60	1.46-1.75	0.95	0.73-1.23

HR = hazard ratio. CI = confidence interval. Baseline and adjusted associations with autism spectrum disorder were assessed in a sample of 1,580,430 offspring. Baseline and adjusted associations with attention-deficit/hyperactivity disorder were assessed in a sample of 1,580,509 offspring. Adjusted models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts. Sibling comparisons controlled for parity and year of birth, paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts, and maternal age at childbearing.

eSupplement H:
Examining Associations Between Dispensations During Later Pregnancy and Offspring Outcomes Among Those with a First-trimester Dispensation

Given that the main analyses focused on first-trimester antidepressant exposure, we conducted a sensitivity analysis to explore whether continued dispensations in the second and/or third trimester was associated with the birth and neurodevelopmental outcomes compared to dispensations only during the first trimester. We defined a group of offspring, labeled Continuers, as those whose mothers had a first-trimester dispensation *and* a second- or third-trimester dispensation. We defined a second group, labeled Discontinuers, as offspring whose mothers had a first-trimester dispensation but not a second- or third-trimester dispensation. Of the 26,477 offspring in the cohort with first-trimester dispensations, 12,291 (46%) were Continuers and 14186 (54%) were Discontinuers. Of the 22,125 offspring with first-trimester dispensations of SSRI specifically, 10,757 (49%) were continuers and 11,368 (51%) were discontinuers.

We examined adjusted associations between continuation of use late in pregnancy and the birth and neurodevelopmental outcomes (eTable 16). The association between continued dispensations of antidepressants and preterm birth (OR = 1.4, 95% CI [1.3, 1.6]) and small for gestational age (OR = 1.2, 95% CI [1.0, 1.4] were statistically significant. The association with autism spectrum disorder was moderate in magnitude (HR = 1.3, 95% CI [1.0, 1.8]), though not statistically significant. Continuation of dispensations was associated with a moderate decrease in the risk for attention-deficit/hyperactivity disorder (HR = 0.8, 95% CI [0.5, 1.1]), but the association was not statistically significant.

These analyses cannot differentiate whether the associations were due to increased severity of depression (i.e., confounding by indication severity) or the intrauterine exposure to antidepressants later in pregnancy.

eTable 16. Adjusted associations between continuation of antidepressant dispensations late in pregnancy and offspring birth and neurodevelopmental outcomes among those with a first-trimester dispensation

	Adjusted Model	
Any antidepressant		
	OR	**95% CI**
Preterm birth	1.44	1.30-1.59
Small for gestational age	1.18	1.01-1.39
	HR	**95% CI**
Autism spectrum disorder	1.32	0.96-1.81
Attention deficit/hyperactivity disorder	0.76	0.53-1.08
SSRIs		
	OR	**95% CI**
Preterm birth	1.39	1.24-1.54
Small for gestational age	1.21	1.01-1.44
	HR	**95% CI**
Autism spectrum disorder	1.22	0.86-1.74
Attention deficit/hyperactivity disorder	0.71	0.47-1.06

OR = odds ratio. HR = hazard ratio. CI = confidence interval. Models predicting outcomes from any antidepressant dispensation were fit in a sample of 26,477 offspring. Models predicting outcomes from SSRIs dispensation were fit in a sample of 22,125 offspring. Models controlled for parity and year of birth and maternal and paternal country of birth, age at childbearing, highest level of completed education, history of any criminal convictions, history of severe psychiatric problems, and history of any suicide attempts.

eReferences

1. Turner LM, Stone WL. Variability in outcome for children with an ASD diagnosis at age 2. *J Child Psychol Psychiatry*.. 2007;48(8):793-802.